Express Mail Label No. EV 604746868 US

Application No. 10/522,356

Page 9 of 13

In the Claims:

Please amend the claims as shown:

1-21. (Canceled)

22. (Previously Added) A method of detecting a gene activation event in a cell in vitro or in

vivo, the method comprising assaying a host cell stably transfected with a nucleic acid construct

comprising a nucleic acid sequence encoding a member of the lipocalin protein family, or a

transgenic non-human animal whose cells express such a construct, in which the cell or animal is

subjected to a gene activation event that is signaled by expression of a peptide tagged lipocalin

reporter gene.

23. (Previously Added) The method of claim 22, wherein the lipocalin protein is

heterologous to the cell in which it is expressed.

24. (Previously Added) The method of claim 22, wherein the lipocalin protein is coded for

by a nucleic acid construct comprising (i) a nucleic acid sequence encoding a member of the

lipocalin protein family, and (ii) a nucleic acid sequence encoding a peptide sequence of from 5

to 250 amino acid residues.

25. (Previously Added) The method of claim 22, wherein the lipocalin is selected from the

group consisting of: ovine betalactoglobulin (BLG) (accession No. X12817), murine major

urinary protein (MUF) (accession No. NM 031188) and rat α -2-urinary globulin (α -2u)

(accession number M27434).

26. (Previously Added) The method of claim 24, wherein the peptide sequence is an epitope.

Express Mail Label No. EV 604746868 US Application No. 10/522,356

Page 10 of 13

- 27. (Currently Amended) The method of claim 26, wherein the epitope is selected from the group consisting of EQKLISEEDL (SEQ ID NO: 1), GKPIPNPLLGLDST (SEQ ID NO: 2), YPYDVPDYA (SEQ ID NO: 3), NVRFSTIVRRRA (SEQ ID NO: 4), KQMSDRRENDMSPS (SEQ ID NO: 5), SGNEVSRAVLLPQSC (SEQ ID NO: 6), SSLSYTNPAVAATSANL (SEQ ID NO: 7), RSTLQHPDYLQEYST (SEQ ID NO: 8), VSTLLRWERFPGHRQA (SEQ ID NO: 9), KFQQLVQCLTEFHAALGAYV (SEQ ID NO: 10), QEQCQEVWRKRVISAFLKSP (SEQ ID NO: 11), and RLSDKTGPVAQEKS (SEQ ID NO: 12).
- 28. (Previously Added) The method of claim 23, wherein the construct additionally comprises a promoter element upstream of the nucleic acid sequence comprising (i) a nucleic acid sequence encoding a member of the lipocalin protein family, and (ii) and nucleic acid sequence encoding a peptide sequence of from 5 to 250 amino acid residues.
- 29. (Previously Added) The method of claim 7, wherein the promoter element is selected from one of the groups consisting of:
- a. c-myc, p21/WAF-1, MDM2, Gadd45, FasL, GAHSP40, TRAIL-R2/DR5, BTG2/PC3;
- b. MnSOD, CuZnSOD, IκB, ATF4, xanthine oxidase, COX2, iNOS, Ets-2, FasL/CD95L, γGCS, ORP150;
- c. Lrg-21, SOCS-2, SOCS-3, PAI-1, GBP28/adiponectin, α-1 acid glycoprotein, metallothioneine I, metallothioneine II, ATF3, IGFbp-3, VDGF, HIF1α;
- d. Gadd 34, GAHSP40, TRAIL-R2/DR5, c-fos, CHOP/Gaddl53, APAF-1, Gadd45, BTG2/PC3, Peg3/Pwl, Siahla, S29 ribosomal protein, FasL/CD95L, tissue tranglutaminase, GRP78, Nur77/NGFI-B, CyclophilinD, p73, Bak;
- e. a promoter from a xenobiotic metabolizing cytochrome p450 enzyme from the 2A, 2B, 2C, 2D, 2E, 2S, 3A, 4A and 48 gene families; and

Express Mail Label No. EV 604746868 US

Application No. 10/522,356

Page 11 of 13

- f. a synthetic promoter sequence comprised of a minimal eukaryote consensus promoter operatively linked to one or more response elements selected from the group consisting of the aryl hydrocarbon (Ah)/Ah nuclear translocator (ARNT) receptor response element, the antioxidant response element (ARE), the xenobiotic response element (XRE).
- 30. (Previously Added) The method of claim 22, wherein the nucleic acid construct comprises a stress inducible promoter operatively isolated from a nucleic acid sequence encoding a member of the lipocalin protein family by a nucleotide sequence flanked by nucleic acid sequences recognized by a site specific recombinase, or by insertion such that it is inverted with respect to the transcription unit encoding a member of the lipocalin protein family, in which the construct additionally comprises a nucleic acid sequence comprising a tissue specific promoter operatively linked to a gene encoding the coding sequence for the site specific recombinase.
- 31. (Previously Added) The method of claim 30, wherein the site-specific recombinase sequences are two *loxP* sites of bacteriophage P1.
- 32. (Previously Added) The method of claim 22, wherein the gene activation event is induction of toxicological stress, metabolic changes, or disease, including a disease that is the result of viral, bacterial, fungal or parasitic infection.
- 33. (Previously Added) A method of screening for, or monitoring of toxicologically induced stress in a cell or a cell line or a non-human animal, comprising the use of a cell, cell line or non human animal which has been transfected with or carries a nucleic acid construct as defined in claim 24.
- 34. (Previously Added) A method for screening and characterizing viral, bacterial, fungal, and parasitic infection comprising the use of a cell, cell line or non human animal which has been transfected with or carries a nucleic acid construct as defined in claim 24.

Express Mail Label No. EV 604746868 US Application No. 10/522,356 Page 12 of 13

35. (Previously Added) A method for screening for cancer, inflammatory disease, cardiovascular disease, metabolic disease, neurological disease and disease with a genetic basis comprising the use of a cell, cell line or non human animal which has been transfected with or carries a nucleic acid construct as defined in claim 24.